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Prediction of Mortality in COVID-19 Patients Using Diagnostic Value of SaO2/FiO2 and PaO2/FiO2 Ratios at Hospital Admission: A Retrospective Cohort Study

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Short Research Article

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ABSTRACT

Background: Approximately 20% of COVID-19 patients have an arterial blood oxygen partial pressure to fractional inspired oxygen concentration ratio (PaO2/FiO2) of less than 300.
Objective: To analyze the diagnostic value of oxygen saturation of arterial blood (SaO2)/FiO2 and PaO2/FiO2 ratios measured upon hospital admission for predicting mortality in COVID-19 patients.
Methods: A retrospective cohort study was conducted at two hospitals in the Central Region of Brazil, involving 199 COVID-19 patients hospitalized from March to August 2020. Data were collected from medical records. Respiratory markers were obtained from blood gas analysis and

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pulse oximetry measurements taken upon admission. Receiver Operating Characteristic curves were constructed to assess the accuracy of the studied ratios in predicting mortality among the analyzed patients.

Results: There were 33 deaths among the total hospitalized COVID-19 patients. Among those with available data on PaO2/FiO2 and SaO2/FiO2 measured upon admission, 22 (20.6%) deaths occurred. Notably, the severity of ARDS correlated with an increased risk of death (p=0.001) within this subgroup. Patients who died had lower PaO2/FiO2 and SaO2/FiO2 ratios compared to survivors. Both PaO2/FiO2 and SaO2/FiO2 ratios measured upon hospital admission were accurate parameters for predicting mortality in COVID-19 patients. The cutoff point of 280 for PaO2/FiO2 and 290 for SaO2/FiO2 showed satisfactory sensitivity in predicting death among the analyzed patients.

Conclusion: SaO2/FiO2 and PaO2/FiO2 ratios measured upon hospital admission exhibited good sensitivity and accuracy in predicting mortality in hospitalized COVID-19 patients. This finding may prove valuable in guiding future pandemic decision-making in healthcare practice and contributing to oxygen management for both non-invasive and invasive ventilation.

Keywords: SaO2/FiO2 ratio; PaO2/FiO2 ratio; Mortality; COVID-19.

1. INTRODUCTION

According to data from the World Health Organization (WHO), more than 767,364,883 cases of COVID-19 have been confirmed worldwide, including 6,938,353 deaths [1]. Approximately 20% of COVID-19 patients are classified as severe cases, characterized by the presence of dyspnea, a respiratory rate exceeding 30 breaths per minute, and an arterial blood oxygen partial pressure to fractional inspired oxygen concentration ratio (PaO_2/FiO_2) of less than 300. The most severe forms of the disease typically manifest in the second week, with dyspnea progressing to severe respiratory failure. Older individuals and those with comorbidities such as diabetes, cardiovascular, and renal diseases are more susceptible to developing acute respiratory distress syndrome (ARDS) [2].

ARDS is characterized by acute lung injury with increased vascular permeability and lung density, which can lead to non-cardiogenic acute pulmonary edema. Its pathophysiology involves acute hypoxemia with a PaO_2/FiO_2 ratio < 300 and is associated with acute pulmonary inflammation. This inflammation results in bilateral lung opacities and increases vascular permeability, leading to a progressive reduction in ventilated lung tissue [3]. The diagnosis of ARDS is based on clinical manifestations, imaging studies, as well as changes in pH values, partial pressure of oxygen (PaO_2), partial pressure of carbon dioxide (PCO_2), and arterial oxygen saturation (SaO_2). Derived parameters from these measures, such as PaO_2/FiO_2 and SaO_2/FiO_2 ratios, can also be altered and used as criteria for diagnosing acute lung injury and ARDS [4] For many years, clinicians have used these ratios as a surrogate for pulmonary shunt fraction [5]. In healthy controls, PaO2/FiO2 ratio varies from 400 to 500 at sea level and reduces with decreasing barometric pressure [6]. There have been studies which show that PaO_2/FiO_2 and SaO_2/FiO_2 ratios are reasonably well correlated in patients with ARDS, particularly when PaO_2/FiO_2 ratios are less than 300 [7-11].

Investigating predictive factors for clinical deterioration of COVID-19 patients is useful in guiding decision-making in healthcare practice and contributes to oxygen management, ranging from non-invasive to invasive ventilation. The objective of this study was to analyze the diagnostic value of SaO_2/FiO_2 and PaO_2/FiO_2 ratios measured upon hospital admission for predicting mortality in COVID-19 patients.

2. MATERIALS AND METHODS

This is a retrospective cohort study aimed at evaluating respiratory functional parameters upon hospital admission in COVID-19 patients and their association with subsequent mortality. The study was conducted from March to August 2020 at two COVID-19 reference hospitals in the Central Region of Brazil, one privately administered and the other publicly administered. Patient selection was based on the positive COVID-19 cases recorded in each hospital unit, confirmed by real-time reverse transcription-polymerase chain reaction (qRT-PCR), rapid antigen testing on nasopharyngeal swabs, IgM/IgG antibody testing against SARS-CoV-2, or a combination of clinical data and chest computed tomography findings consistent with

respiratory changes caused by the novel coronavirus.

Demographic and clinical data were obtained from the medical records of the evaluated hospitals. Information about comorbidities was considered if recorded during the patient's first medical interview upon admission. Respiratory function markers were analyzed through arterial blood analysis and pulse oximetry measurements taken on the patient's admission date, serving as baseline information. The results of PaO_2, SaO_2, and FiO_2 from the patient's admission blood gas analysis were used to calculate the PaO2/FiO2 and SaO_2/FiO_2 ratios. The definition of ARDS followed the Berlin criteria of 2012 [12] and its severity was classified according to Falavigna et al., 2020 as mild (PaO_2/FiO_2 between 300 and 200), moderate (PaO_2/FiO_2 between 200 and 100), or severe (PaO_2/FiO_2 less than or equal to 100) [13].

Receiver Operating Characteristic (ROC) curves were constructed to assess the sensitivity and specificity of SaO_2/FiO_2 and PaO_2/FiO_2 ratios determined upon hospital admission for predicting the occurrence of mortality in COVID-19 hospitalized patients. The areas under the curve (AUC) were calculated to demonstrate the accuracies of these markers. The Youden's J Index was calculated to define empirical cutoff points corresponding to sensitivity and specificity values least likely to have occurred by chance. A significance level of alpha error at 0.05 was considered statistically significant for the analyzed variables. Statistical analyses were performed using Stata 12.0 software (Stata Corporation, College Station, TX, USA).

3. RESULTS

A total of 199 COVID-19 patients hospitalized from March to August 2020 were included in the study. Of these, 133 (66.8%) were admitted to a private hospital, and 66 (33.2%) to a public hospital. Most patients were over 50 years old, male, residents of the metropolitan area of Cuiabá (MT), with a medium to high level of education, and of white or mixed race. Among the included patients, 122 comorbidities were recorded, with the most common being arterial hypertension (40.2%), diabetes mellitus (22.6%), and obesity (18.6%). A diagnosis of ARDS was registered in 40 patients, with 21 (52.5%) classified as mild ARDS, 10 (25.0%) as moderate ARDS, and 9 (22.5%) as severe ARDS. Of the total COVID-19 hospitalized patients, 33 (16.6%) progressed to death, of which 22 (20.6%) were part of a group of 107 and 101 patients with available information on PaO_2/FiO_2 and SaO_2/FiO_2 measured upon hospital admission, respectively. In this latter group of patients, there was a progressive increase (p=0.001) in the proportion of deaths according to the severity of ARDS. Upon hospital admission of the patients, the median (quartile 1; quartile 3) for PaO_2/FiO_2 was 353 (237; 465), and for SaO_2/FiO_2 was 352 (279; 471). Lower PaO_2/FiO_2 and SaO_2/FiO_2 ratios were observed among patients who died compared to those who survived (Table 1).

Table 1. Distribution of deaths of patients hospitalized with COVID-19 according to the clinical stage of ARDS and according to the PaO2/FiO2 and SaO2/FiO2 ratios measured at patient admission

Clinical feature	Death		Total	p
	YES n (%)	NO n (%)	Median (Q1; Q3)	
ARDS stage				
Without ARDS (n=61)	7 (11.5%)	54 (88.5%)	61	0.001*
Mild (n=21)	5 (23.8%)	16 (76.2%)	21	
Moderate (n=10)	4 (40.0%)	6 (60.0%)	10	
Severe (n=9)	6 (66.7%)	3 (33.3%)	9	
Respiratory biomarker	**Median (Q1; Q3)**	**Median (Q1; Q3)**		
$PaO_2/FiO2$ (n=101)	225 (98; 429)	364 (280; 483)	353 (237; 465)	0.001**
SaO_2/FiO_2 (n=107)	241 (102; 340)	392 (321; 475)	352 (279; 471)	<0.001**

Q1: First quartile
Q3: Third quartile
**: Qui-quadrado for linear trend.*
***: Mann-Whitney U test*

Fig. 1. ROC curve of the accuracy of the PaO2 /FiO2 [A] and SaO2 /FiO2 [B] ratio with potential diagnostic value for the outcome of death in patients hospitalized with COVID-19 from March to August 2020

The ROC curves constructed from the studied ventilatory parameters showed high AUC values for both PaO_2/FiO_2 (72.7%) and SaO_2/FiO_2 (73.1%) measured upon hospital admission, for predicting mortality in this group of patients. The cutoff point of 280 for PaO_2/FiO_2 had satisfactory sensitivity (77.2%), specificity (68.2%), and accuracy (75.3%) for predicting death, and similarly, the cutoff point of 290 for SaO_2/FiO_2 showed high sensitivity (82.4%), specificity (59.1%), and accuracy (77.6%) for predicting death among the analyzed patients (Fig. 1).

4. DISCUSSION

The results of this study demonstrate that hospitalized COVID-19 patients are more likely to die if they are in more severe stages of ARDS or have low PaO2/FiO2 and/or SaO_2/FiO_2 ratios upon hospital admission. Furthermore, the determination of PaO_2/FiO_2 and SaO_2/FiO_2 ratios at admission showed satisfactory accuracy for predicting mortality in hospitalized COVID-19 patients.

The association between COVID-19 mortality and ARDS severity has been reported in previous studies and is directly related to the greater extent of respiratory compromise [14,15]. It is also well-established that a low PaO_2/FiO_2 ratio is significantly associated with hospital mortality in COVID-19 patients [16,17]. $PaO2/FiO_2$ levels below 200 have been identified as predictors of higher mortality risk and shorter survival time in patients with severe ARDS [18]. In another study, a low PaO_2/FiO_2 ratio at admission in COVID-19 patients in intensive care units was found to be a predictor of mortality in a study conducted in Colombia [19]. On the other hand, variation in SO_2/FiO_2 ratio can be very useful for the continuous monitoring and prognosis COVID-19 critical patients [20].

It is important to highlight that the severity of COVID-19 cannot be solely attributed to the repercussions of lung injury on blood gases. Although the buffer capacity of blood is important for acid-base homeostasis in the body, it is not often considered a primary factor in determining the severity of COVID-19. However, recently, Garai & Gorai (2020) proposed a new interpretation for the effects of COVID-19 on pH and blood gas homeostasis. Factors related to SARS-CoV-2, which utilizes amino acids, proteins, and inorganic chemicals for its survival and replication in human blood, negatively impact blood pH and buffering capacity. The lower the blood buffering capacity, the worse the maintenance of acid-base balance. The lower the pH, the greater the severity and mortality of COVID-19 [21].

The main limitation of the presented results was the loss of information for a significant portion of COVID-19 patients hospitalized, primarily due to inadequate record-keeping in medical records.

5. CONCLUSION

SaO_2/FiO_2 and PaO_2/FiO_2 ratios measured upon hospital admission are reduced, with more pronounced reductions observed in COVID-19 patients with a greater chance of progressing to moderate or severe ARDS. These two ratios exhibit good accuracy in predicting mortality in hospitalized COVID-19 patients. The study findings may prove valuable in guiding future pandemic decision-making in healthcare practice and contributing to oxygen management for both non-invasive and invasive ventilation.

CONSENT

It is not applicable.

ETHICAL APPROVAL

This study was approved by the Ethics and Research Committee of Hospital Universitário Júlio Muller (HUJM) on September 1, 2020, under approval number 4252218.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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